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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/633,629	08/05/2003	Ayoub Rashtchian	38266-0009	6375

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EXAMINER	
POPA, ILEANA	
ART UNIT	**PAPER NUMBER**
1633	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/04/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/633,629	RASHTCHIAN ET AL.	
	Examiner	Art Unit	
	Ileana Popa	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 October 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) *5,6,19 and 20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,7-18 and 21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in the prior Office Action.

2. Claims 5, 6, 19, and 20 have been withdrawn.

Claims 1-4, 7-18, and 21 are under examination.

Response to Arguments

Double Patenting

3. Claim 1 remain provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 17 of co-pending Application No. 10/766,312 because Applicant did not submit a terminal disclaimer.

35 USC § 102

4. The rejection of claims 1-4, 11, and 15-18 under 35 USC § 102(b) as being anticipated by Li et al. (Brain Research Protocols, 2000, 5: 211-217), as evidenced by www.dermaxime.com/alcohol.htm is withdrawn in response to Applicant's arguments filed on 10/12/2006 and in response to the fact that the art teaches that glycerol stabilizes air bubbles.

5. Claims 1, 8, 11, and 12 remain rejected under 35 USC § 102(b) as being anticipated by Stemmer et al. (U.S. Patent No. 5,834,252). Applicants' arguments filed on 10/12/2006 have been fully considered but they are not fully persuasive.

Applicant traversed the instant rejection on the grounds that the reference to antifoam agents occurs in a paragraph that intends to define physiological conditions and states that other agents may optionally be added such as divalent cations, metal chelators, nonionic detergents, membrane fractions, antifoam reagents, and scintillants. Applicant argues that this is an unreliable source of information regarding PCR reactions. Applicant submits that it is well known in the art that PCR is highly sensitive with respect to the nature and concentration of divalent cation concentration; however, Stemmer et al. suggest extremely broad divalent cations ranges and indicate that Ca2+ would be suitable, even though this would result in no PCR product. Moreover, Applicant argues, a paragraph suggesting the inclusion of a chelating agent that would result in complete reaction inhibition would not suggest to one of skill in the art the use of antifoam, let alone suggest either the identity of a suitable antifoam or appropriate concentration of the antifoam. Applicant argues that neither the more detailed discussion in PCR reaction conditions, nor the specific examples contain any mention whatsoever of antifoam reagents, nor do they suggest that addition of antifoam agents would be either useful or desirable. Therefore, Applicant requests the withdrawal of the rejection.

Contrary to Applicant' assertions, the level of skill in the art is such that one of skill in the art would readily recognize suitable PCR conditions. Therefore, one of skill in

the art would have known not to use undesirable reagents such as chelator agents in PCR, this was common knowledge in the art before the invention was made. On the other hand, one of skill in the art would have readily recognized the utility of using antifoam agents in PCR, especially that the art teaches that proteins (i.e., polymerases) could be inactivated by foaming. Therefore, one of skill in the art would have been motivated to use antifoaming agents to improve PCR efficiency by reducing enzyme degradation. With respect to the argument that the paragraph in Stemmer et al. does not identify a suitable antifoam and concentration to be used in PCR, it is noted that the rejected claims are broadly drawn to any antifoam agents and no concentration is mentioned. The fact that Stemmer et al. do not provide examples of using such agents is irrelevant since choosing the right antifoam agent and the appropriate concentration is nothing but optimization that can be achieved by routine experimentation. For these reasons the claimed invention is anticipated by Stemmer et al.

6. The rejection of claims 1-4, 11, and 15-18 under 35 USC § 102(e) as being anticipated by Heid et al. (U.S. Patent No. 6,358,679), as evidenced by www.dermaxime.com/alcohol.htm is withdrawn in response to Applicant's arguments filed on 10/12/2006 and in response to the fact that the art teaches that glycerol stabilizes air bubbles.

35 USC § 103(a)

7. Claims 1-4, 7, 11, 15-18, and 21 remain rejected under 35 USC § 103(a) as

being unpatentable over Blaschke et al. (J Immunol Methods, 2000, 246: 79-90), in view of each Stemmer et al., Varadaraj et al. (Gene, 1994, 140:1-5, Abstract), and Swerdlow et al. (Anal Chem, 1997, 69: 848-855). Applicants' arguments filed on 10/12/2006 have been fully considered but they are not fully persuasive.

Applicant traversed the instant rejection on the grounds that both the suggestion/motivation and a reasonable expectation of success must be found in the prior art, and not inferred from Applicant's disclosure. Applicant submits that the Examiner has failed to describe why one of ordinary skill in the art would have been motivated to combine the cited references, and has failed to provide appropriate evidence that there was a reasonable expectation of success in making the combination. Applicant argues that although Varadaraj et al. may suggest that in certain circumstances some detergents may be added to a PCR, they state that ethanol inhibited PCR amplification. Since the site cited by the Examiner discloses that ethanol is also an antifoam, the result of Varadaraj et al. confirm the findings in the present application that certain antifoams are deleterious to PCR. Applicant concludes that Varadaraj et al. teach away from the invention and confirms the surprising nature of the results obtained by Applicant that certain antifoams at particular concentrations can be used in PCR without inhibiting the reaction. Regarding Swerlow et al., Applicant argues that it is not clear what causes bubbles in their method, because a detergent was not used by them. Applicant argues that the bubbles could have been generated after the PCR reaction during the liquid flow from the PCR reaction to the chromatography column and in this case there would have been no motivation to add an antifoam to the

PCR reagent. Regarding Blaschke et al., Applicant argues that they specifically describe single band PCR products (p. 83, column 2) and therefore one of skill in the art would have had no motivation to modify their teachings as stated in the prior Office action because they teach obtaining very good results in the absence of any foam-causing detergent. Additionally, Applicant argues that Stemmer is not enabling for the reasons above. Therefore, since nothing in the combination of cited references would have motivated one of skill in the art to use an antifoam reagent in a PCR reaction and Applicant requests the withdrawal of the rejection.

Contrary to Applicant's assertion, one of skill in the art would have been motivated to modify the method of Blaschke et al. by adding detergent because Varadaraj et al. teach that addition of detergents improves the specificity of the amplified products, especially when one deals with G+C-rich DNAs. Even if Blaschke et al. teach obtaining good specificity for DNA encoding for cytokines, it is noted that one of skill in the art would have known that the method of Blaschke et al. could be used for any other DNA, including G+C-rich DNAs and therefore, one of skill in the art would have known to improve PCR specificity by using detergents, as taught by Varadaraj et al. Swerdlow et al. was used only because they teach the need to eliminate the air bubbles before detection by laser-induced fluorescence. Therefore, one of skill in the art would have been aware of the need to eliminate the air bubbles before detection and moreover, one of skill in the art would have known to use antifoam agent as an alternative, because Stemmer et al. teach their use in PCR (see above). With respect to the argument that Varadaraj et al. teach away from the invention, it is noted that

Varadaraj et al. do not teach that all antifoam agents inhibit PCR. Stemmer et al. do teach the use of antifoam agents in PCR and therefore one of skill in the art would have known that not all antifoam agents are inhibitory and would have been able to identify the adequate antifoam agents by routine experimentation and therefore. Since only routine experimentation is required to achieve this, one of skill in the art would have been expected to have a reasonable expectation of success in doing such. For these reasons the claimed invention was *prima facie* obvious at the time the invention was made.

8. Claims 1, 9, 11, and 13 remain rejected under 35 USC § 103(a) as being unpatentable over Stemmer et al., in view of Kyle (U.S. Patent No. 5,658,787). Applicants' arguments filed on 10/12/2006 have been fully considered but they are not fully persuasive.

Applicant traversed the instant rejection on the grounds that Stemmer is not enabling for the reasons presented above and that Kyle teaches fermentation, not PCR and there would have been no motivation to combine these two disparate references. Applicant argues that one of skill in the art would not have been motivated to refer to a patent describing fermentation methods to identify a solution to a problem with PCR and that there is nothing in either Stemmer et al. or Kyle that would have provided one of ordinary skill in the art to use any antifoam, let alone 1520-US. Therefore, Applicant requests the withdrawal of the rejection.

Contrary to Applicant's assertion Stemmer et al. do teach the use of antifoam

agents in PCR and one of skill in the art would have been motivated to use antifoaming agents to improve PCR efficiency by reducing enzyme degradation (see above). Given the teachings of Stemmer et al., one of skill in the art would have been motivated to look for antifoam agents known in the art. By doing this, one of skill in the art would have necessarily identified, among others, Kyle's patent that teaches 1520-US as a very efficient antifoamer. Therefore, one of skill in the art would have been motivated to use it in PCR and would have been able to do this with a reasonable expectation of success by routine experimentation. For these reasons, the claimed invention was *prima facie* obvious at the time the invention was made.

9. Claims 1 and 8-14 remain rejected under 35 USC § 103(a) as being unpatentable over Stemmer et al. taken with Kyle, in further view of Sigma catalog (1998) and Wieranga (U.S. Patent No. 5,968,889). Applicants' arguments filed on ... have been fully considered but they are not fully persuasive.

Applicant traversed the instant rejection on the grounds that the deficiencies of Stemmer et al. and Kyle are not cured by either Sigma catalog or Wieranga because neither teaches or suggests the use of antifoamers in PCR. Applicant argues that one of skill in the art would not have been motivated to use Wieranga, which deals with the problem of foaming when using household dishwasher detergents in high concentration, in an attempt to solve a problem in PCR that uses different detergents at vastly lower concentration. Applicant argues that neither of the references provides any motivation to use combinations of antifoamers in PCR, nor do they provide any indication that the

combination would be successful. Therefore, Applicant requests the withdrawal of the rejection.

Contrary to Applicant's assertion, as noted above, one of skill in the art would have been motivated to look for antifoam agents known in the art. By doing this, one of skill in the art would also have necessarily identified Wieranga, who teaches that combinations of silicone-based (i.e., 1520-US) and organic antifoamers act synergistically. The fact that Wieranga teaches this combination for dishwasher detergents is irrelevant since the art teaches that antifoamers can be used for many other applications where foam removal is needed (see for example Kyle above). Therefore, one of skill in the art would have been motivated to test the use a combination as taught by Wieranga in PCR and would have been able to identify this combination as suitable for PCR with a reasonable expectation of success by routine experimentation. For these reasons, the claimed invention was *prima facie* obvious at the time the invention was made.

Conclusion

10. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ileana Popa whose telephone number is 571-272-5546. The examiner can normally be reached on 9:00 am-5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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